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Formulation and In-Vitro Evaluation of Topical Emulgel of Phenyl Benzoate by Using Different Polymers

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A B S T R A C T

The objective of the present investigation was to formulate and in vitro evaluation of topical emulgel of phenyl benzoate by using different polymers. Topical drug administration is simplest and easiest route of localised drug delivery anywhere in the body by routes as ophthalmic, rectal, vaginal and skin. Phenyl Benzoate binds to and inactivates prostaglandin H synthase through peroxide mediate deactivation then reduced production of prostaglandin leads to reduced inflammation of the surrounding tissues. Twelve formulations of topical emulgel was preparing the emulsion and its jellification by mixing with the gel solution with polymer such as Carbapol 934, Tween-80, Span-80, ethanol, methyl paraben, propyl paraben, HPMC, wheat germ oil and thyme oil in different ratios. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, spreadability, consistency and viscosity. Out of all the formulation developed formulation F3formulation to show the highest value when compared to other formulations.

Keywords: Phenyl benzoate, Emulgel, Carbapol, Formulation, Methyl Paraben, HPMC

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder directly. The spectrum of drugs/agents applied directly to the skin ranges from anti-inflammatory, antiseptic, antibacterial, antifungal, antiviral, anti-acne, anti- pigmentary, anesthetic compounds to skin emollients and protectants. Topical route has the main advantage of

direct delivery of drug to the target tissue i.e. skin and mucous membranes, bypassing the firs-pass effect.

Topical formulations can vary in consistency from solid, semisolid to liquid depending on their physicochemical properties. Besides the active substance (drug), each formulation has many non-medicinal ingredients (excipients) with diverse pharmacological functions. Sometimes more than one formulation can be combined to enhance the drug delivery. Topical drug administration is simplest and easiest route of localised drug delivery anywhere in the body by routes as ophthalmic, rectal, vaginal and skin. These are applied as a wide spectrum of preparations in case of both cosmetic and dermatological, to the healthy or diseased skin. The formulations are available in different forms like from solid through semisolid to liquid. Drugs are administered topically for their action at the site of application or for systemic effects. When a classical gel formulation is combined with an emulsion is called an EMULGEL.

Preparation of Emulgel:

Emulgel was prepared by the method reported with minor modification. The Gel in formulations were prepared by dispersing Carbopol 934 in purified water with constant stirring at a moderate speed and Carbopol 940 in purified water with constant stirring at a moderate speed then the pH are adjusted to 6 to 6.5 using triethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving Span 80 in light liquid paraffin having the drug in ethanol solution while the aqueous phase was prepared by dissolving Tween 80 in purified water. Methyl and Propylparaben was dissolved in propylene glycol and were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70 ° to 80 °C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. And add glutaraldehyde in during of mixing of gel and emulsion in ratio 1:1 to obtain the Emulgel.

Drug Profile:

Phenyl Benzoate is a synthetic, pyrazoline derivative. it is non hormonal anti-inflammatory, antipyretic compound useful in the management of inflammatory conditions. The apparent analgesic effect is probably related mainly to the compounds anti-inflammatory properties and arise from its ability to reduce production prostaglandin H and prostacyclin. Prostaglandins act on a variety of cells such as vascular smooth muscle cells causing constriction or dilation, on platelets causing aggregation or disaggregation and on spinal neurons causing pain. Prostacyclin causes vascular constriction platelet disaggregation.

2. Materials and Methods

Construction of Calibration Curve for Phenyl benzoate:

Preparation of acetate buffer pH 5.512: -Acetate buffer was chosen to simulate the human skin pH condition of 5.5.To prepare 1000 ml of the acetate buffer solution, 150 g of sodium acetate was dissolved in 250 ml of distilled water. Exactly 15 ml of glacial acetate acid was then added very slowly into the sodium acetate aqueous solution. Finally, the volume was made with distilled water.

Preparation of BTM releasing medium. Composition - 95% v/v acetate buffer and 0.5% v/v tween 80 and3% v/v methanol

Preparation of Standard Drug Solution:

Stoke I solution: 100mg of Phenyl benzoate was dissolved in 100 ml of acetate buffer pH 5.5, to get a solution of 1000µg/ml concentration. Standard solution: 10ml of stoke I solution was made to 100ml with acetate buffer pH 5.5, thus giving a concentration of 100 g/ml. again 10ml of this stock II solution was made to 100ml with acetate buffer 5.5. Aliquot of standard drug solution ranging from 1 to 10 ml were transferred in to 10 ml volumetric flask and were diluted up to the mark with acetate buffer pH 5.5. Thus, the final concentration ranges from 1-10 g/ml. Absorbance of each solution was measured at 426.0 nm against acetate buffer pH 5.5 as a blank.

Preformulating Studies:

Before formulation of drug substances into a dosage form, it is essential that drug and polymer should be chemically and physically characterized. Preformulating studies give the information need to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excipients in the fabrication of a dosage form.

Drug-excipient interaction study:

This was carried out to check the compatibility between drug and various polymers. It is therefore necessary to confirm that drug is not interacting with polymers under experimental conditions and shelf life. In the present analysis it was carried out by FTIR analysis.

Fourier Transform Infrared Spectrophotometry (FTIR)88-90: Compatibility study of drug with the excipients was determined by FTIR Spectroscopy. The pellets were prepared at high compaction pressure by using KBr and the ratio of sample to KBr is 1:100. The pellets thus prepared were examined and the spectra of drug and other ingredients in the formulations were compared with that of the original spectra. Phenyl benzoate emulgels are prepared by preparing the emulsion and its jellification by mixing with the gel solution.

Preparation of emulsion:

Oil phase was prepared by dissolving span 20 in liquid paraffin. Aqueous phase was prepared by the following steps. Tween 20 was dissolved in distilled water. Drug was dissolved in ethanol. Propyl and methyl parabens were dissolved in propylene glycol. Later two solutions were added to the former solution and mixed well. Both the oil and aqueous phases are separately heated to 60-700 C and then oil phase is added to the aqueous phase with continuous stirring. Stirring is continued until it reached the room temperature.

Preparation of gel solution:

Gel was prepared by simply dispersing the corresponding gelling agent in distilled water.

Mixing of both in 1:1 ratio:

Finally, the emulsion and the gel were mixed in 1:1 ratio with gentle stirring and the Emulgel was obtained. The gel for formulations F1, F2, F3, F4, was prepared by dispersing Carbopol 940 in with constant stirring at moderate speed and after the addition of emulsion, 1-2 drops of TEM

(triethanolamine) was added and mixed thoroughly to get the final Emulgel. The gel for the formulations F5, F6, F7, F8, was prepared by disoarsing HPMC K4M in purified water and for F9, F10, F11, F12, was prepared by dispersing Na. alginate in purified water.

Evaluation of the Prepared Topical Phenyl benzoate Emulgel:

Physical appearance: The prepared Phenylbutazone Emulgel formulations were inspected visually for their color, homogeneity, texture.

pH determination: 1% aqueous solutions of the Emulgels were prepared and the pH was checked with a digital pH meter.

Consistency: This is done by using the consistency tester. One of the criteria for an Emulgel to meet the ideal quantities is that it should possess good spreadability which depends upon the consistency. It is term expressed to denote the extent area to which gel readily spread on application to skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value.

Spreadability

It is expressed in terms of time in seconds taken by the slide to move from A to B from 1gm of Emulgel placed beneath the slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability. It is calculated by using the formula.

$$S = M. L / T$$

Where M = weight tied to upper slide L = Distance between A and B

T = time taken to separate the slides

Viscosity: Viscosityis a physical property of fluids. It shows resistance to flow. In a simple example, water has a low viscosity, as it is "thin". Syrup and tar, on the other hand, have a high viscosity, as they are "thick".

Drug Content Determination:

Drug concentration in Emulgel was measured by UV spectrophotometer. Phenyl benzoate content in Emulgel was measured by dissolving 5ml quantity of Emulgel in 100ml acetate buffer. Absorbance was measured after suitable dilution at 426 nm in UV/VIS spectrophotometer.

In-vitro drug release of Phenyl benzoate:

The in vitro release of Phenyl benzoate from the gel formulation was studied by open ended cylinder method. This diffusion cell apparatus consists of a glass tube with an inner diameter of 2.5 cm, open at the both ends. one end of the tube tied with start-M-membrane, which serve as a donar compartment. 1 gm of Phenyl benzoate gel was taken in this compartment and placed in a beaker containing 200 mi of5.5 P^H of acetate buffer was replaced into the diffusion medium to maintain the sink condition through out of experimentation. Then the sample assayed by spectrophotometrically at 225nm in UV-spectrophotometer using 5.5 P^H of acetate buffer as blank.

Table 1: List of Materials

Name	Source	Grade
Xanthane Gum	Simhapuri Chemicals	Laboratory Reagent
Phenyl Benzoate	Tci Chemicals	Laboratory Reagent
Tween -80	Avra	Laboratory Reagent
Span-80	Oxford Labfine Chem.Llp	Laboratory Reagent
Ethanol	Simhapuri Chemicals	Analytical Reagent
Carbapol -934	Oxford Labfine Chem Llp	Laboratory Reagent
Propylin Glycol	Nice Chemicals (P)Ltd	Laboratory Reagent
Methyl Paraben	Nice Chemicals(P)Ltd	Laboratory Reagent
Propyl Paraben	Oxford Labfine Chem Llp	Laboratory Reagent
HPMC	Simhapuri Chemicals	Analytical Reagent
Wheat Germ Oil	Afromeal	Laboratory Reagent
Thyme Oil	Naturoman International	Laboratory Reagent

Table 2: List of Equipment's

Equipment Name	Manufacture	Source
FTIR Spectroscopy	Acmas Technologies	Japan
Single Pan Digital Balane	Himalaya Precision Balances	Japan
Uv-Visible Spectrophotometry Double Beam	Double Beam Uv-Vis Spectrophotometer -2377 Electronics	Hyderabad
Magnetic Stirrer	Remi Magnetic Stirrers	Hyderabad
Mechanical Stirrer	Star Scientific Instruments	Hyderabad

3. Results and Discussion

Based on the experimental methods, the results are arranged in the order of Construction of Calibration Curve for Phenyl Benzoate, FT-IR (Fourier Transform Infrared Spectrophotometry, Physical examination, pH determination, Consistency, Drug content determination, *Ex vivo* diffusion study, Skin deposition study, and Skin Irritation test.

Construction of Calibration Curve for drug Phenyl Benzoate at λmax 426nm: The absorbances were measured by taking 1 µg/ml, 2 µg/ml, 3µg/ml, 4µg/ml, 5µg/ml, 6µg/ml, 7µg/ml, 8µg/ml, 9µg/ml, 10µg/ml as the serial concentrations spectrometric ally at 426 nm.

Table 3: Spectrophotometric data for the estimation of Phenyl Benzoate

Concentration (g/ml)	Absorbance (λmax 426nm)
1	0.045
2	0.084
3	0.093
4	0.154
5	0.204
6	0.216
7	0.251
8	0.286
9	0.322
10	0.351

Physical Examination: The prepared Phenyl Benzoate Emulgel formulations were yellow viscous creamy preparations with a smooth and homogeneous appearance.

pH testing: The pH values of all the prepared formulations ranged from 5.5 to 6.5.

Table 4: pH data of Phenyl Benzoate

Formulation	pH
F1	6.5
F2	6.1
F3	6.3
F4	6.1
F5	6.5
F6	6.4
F7	6.4
F8	6.1
F9	5.4

Table 5: Data of consistency of the prepared Emulgels

Formulation code	Time taken for the movement from A to B (sec)
F1	2
F2	3
F3	4
F4	3
F5	4
F6	5
F7	2
F8	3
F9	4

Table 6: Viscosity data

Formulation	Viscosity
F1	41,000
F2	43,000
F3	51,000
F4	36,000
F5	40,000
F6	42,000
F7	38,000
F8	41,000
F9	42,000

Drug Content Determination: The drug content values for all the formulations are represented as following in term of percentages.

Table7: Entrapment efficiency data for the prepared Emulgel

Formulation	Entrapment efficiency
F1	85%
F2	82%
F3	90%
F4	87%
F5	83%
F6	82%
F7	81%
F8	82%
F9	75%

Diffusion studies:

The release profiles of Phenyl Benzoate through the start M-membrane from its various Emulgel formulations are represented as following.

Table 8: Cumulative amount of drug release

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
30	2.03	2.81	4.50	2.65	3.18	3.50	2.41	2.36	3.67
60	9.34	13.34	15.53	10.67	10.75	14.50	5.44	6.88	9.67
90	14.17	18.74	20.96	13.88	16.64	18.96	7.25	7.67	11.88
120	15.77	23.39	25.69	15.90	20.46	24.69	9.23	13.47	14.90
150	19.76	25.11	27.46	19.64	23.30	28.46	11.41	14.83	18.64
180	22.19	25.77	28.24	22.85	24.04	30.34	13.88	18.37	20.85
210	25.11	30.75	33.34	25.07	31.86	38.34	16.72	19.56	24.09
240	29.06	38.57	41.33	27.97	34.87	40.42	19.60	23.10	28.75
270	31.66	41.48	46.88	32.73	36.53	45.55	22.60	25.69	31.70

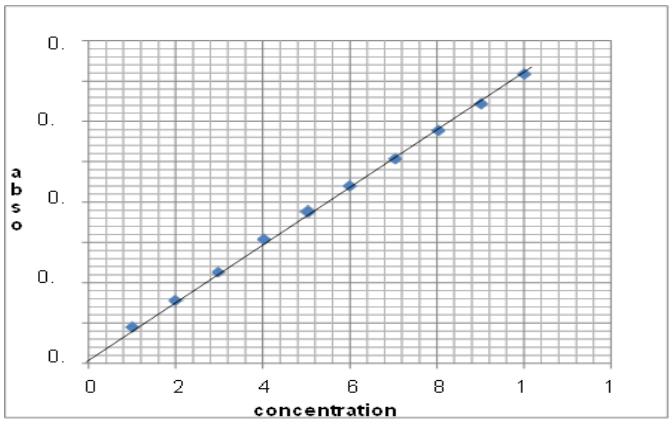

Fig 1: Calibration curve for the estimation of drug Phenyl Benzoate

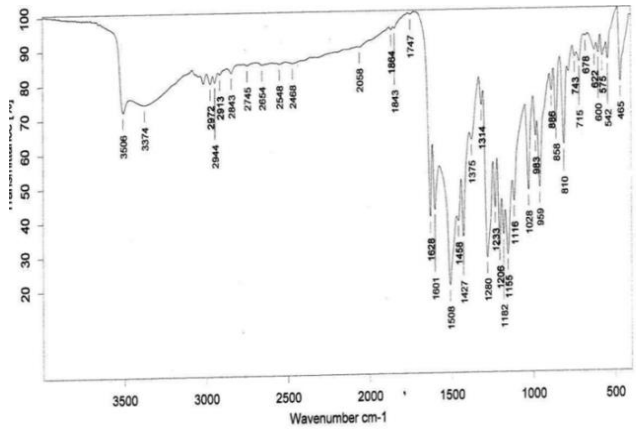

Fig 2: Drug spectrum of Phenyl Benzoate

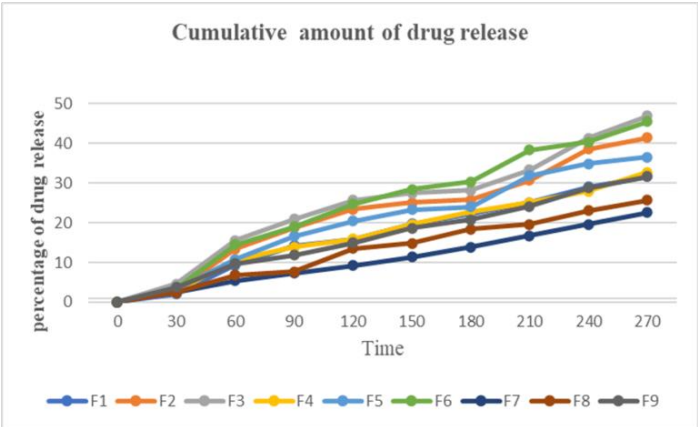

Fig 3: Cumulative amount drug release of Phenyl Benzoate

Phytochemical analysis:

Tablet 1: Phytochemical Analysis

Name of Phytoconstituents	Name of test	Result
Alkaloids	Mayor‘s test	+ve
Flavonoids	By magnesium ribbon	+ve
Amino acids	Ninhydrin test	+ve
Tannins	Ferric chloride test	+ve
Saponins	Froth test	+ve
Steroids	By using sulphuric acid	-ve
Carbohydrates:	Fehling’s test	+ve
Terpenoids	Salkowski test	+ve
Chalcones	By using ammonium hydroxide	-ve

4. Conclusion

The topical Phenyl Benzoate Emulgels were prepared and evaluated. All the formulations showed acceptable physical properties, pH, consistency, drug diffusion, deposition. In drug release studies, Emulgels were compared with respect to concentrations of oil phase, emulsifier, and type of gelling agent. The Carbopol-based Emulgel with the Thyme oil and the emulsifying agent in its high level proved to be the formula of choice since it showed the highest drug release and drug deposition. Drug content entrapment efficiency of F3 formulation to show the highest value when compared to other formulations.

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